BLOOD RESEARCH
VOLUME 49 · NUMBER 1
March 2014
ORIGINAL ARTICLE

Clinical features and treatment outcomes in patients with mantle cell lymphoma in Korea: Study by the Consortium for Improving Survival of Lymphoma

Byung Woog Kang[1], Sang Kyun Sohn[1#], Joon Ho Moon[1], Yee Soo Chae[1], Jong Gwang Kim[1], Soo Jung Lee[1], Won Seog Kim[2], Je-Jung Lee[3], Se Ryeon Lee[4], Keon Uk Park[5], Ho Sup Lee[6], Won Sik Lee[7], Jong-Ho Won[8], Moo-Rim Park[9], Jae-Yong Kwak[10], Min Kyoung Kim[11], Hyo Jung Kim[12], Sung Yong Oh[13], Hye Jin Kang[14], Cheolwon Suh[15#]

Department of Hematology/Oncology, Internal Medicine, [1]Kyungpook National University Hospital, Daegu, [2]Samsung Medical Center, Seoul, [3]Chonnam National University Hwasun Hospital, Hwasun, [4]Korea University Ansan Hospital, Ansan, [5]Keimyung University Dongsan Medical Center, Daegu, [6]Kosin University Gospel Hospital, Busan, [7]Inje University Busan Paik Hospital, Busan, [8]Soonchunhyang University Hospital, Seoul, [9]Wonkwang University Hospital, Iksan, [10]Chonbuk National University Hospital, Jeonju, [11]Yeungnam University Medical Center, Daegu, [12]Hallym University Scared Heart Hospital, Anyang, [13]Dong-A University Hospital, Busan, [14]Korea Cancer Center Hospital, Seoul, [15]Asan Medical Center, Seoul, Korea

p-ISSN 2287-979X / e-ISSN 2288-0011
http://dx.doi.org/10.5045/br.2014.49.1.15
Blood Res 2014;49:15-21.

Received on October 29, 2013
Revised on December 5, 2013
Accepted on February 19, 2014

[#]Cheolwon Suh and Sang Kyun Sohn contributed equally to this work.

Correspondence to
Cheolwon Suh, M.D., Ph.D.
Sang Kyun Sohn, M.D., Ph.D.
C.S., Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, 88, Olympic-ro 43-gil, Songpa-gu, Seoul 138-736, Korea
S.K.S., Department of Hematology/Oncology, Kyungpook National University Hospital, Kyungpook National University School of Medicine, 200, Dongduk-ro, Jung-gu, Daegu 700-712, Korea
Tel: C.S., +82-2-3010-3209
S.K.S., +82-53-420-5587
Fax: C.S., +82-2-3010-6961
S.K.S., +82-53-426-2046
E-mail: C.S., csuh@amc.seoul.kr
S.K.S., sksohn@knu.ac.kr

Background
We investigated the clinical features and treatment outcomes of patients with mantle cell lymphoma (MCL) in Korea.

Methods
We retrospectively analyzed the clinical characteristics and prognosis of 131 patients diagnosed with MCL between January 2004 and December 2009 at 15 medical centers in Korea; all patients received at least 1 chemotherapeutic regimen for MCL.

Results
The median age for the patients was 63 years (range, 26–78 years), and 77.9% were men. A total of 105 patients (80.1%) had stage III or IV MCL at diagnosis. Fifty-two patients (39.7%) were categorized with high- or high-intermediate risk MCL according to the International Prognostic Index (IPI). Eighteen patients (13.7%) were in the high-risk group according to the simplified MCL-IPI (MIPI). The overall incidence of extranodal involvement was 69.5%. The overall incidence of bone marrow and gastrointestinal involvements at diagnosis was 41.2% and 35.1%, respectively. Cyclophosphamide, doxorubicin, vincristine, prednisolone, and rituximab were used frequently as the first-line treatment (41.2%). With a median follow-up duration of 20.0 months (range, 0.2–77.0 months), the overall survival (OS) at 2 years was 64.7%, while the event-free survival (EFS) was 39.7%. Multivariate analysis showed that the simplified MIPI was significantly associated with OS. However, the use of a rituximab-containing regimen was not associated with OS and EFS.

Conclusion
Similar to results from Western countries, the current study found that simplified MIPI was an important prognostic factor in Korean patients with MCL.

Key Words Mantle cell lymphoma, Epidemiology, Trend, Survival, Chemotherapy, Rituximab

INTRODUCTION

Mantle cell lymphoma (MCL) is a distinct subtype of B-cell lymphoma and comprises approximately 5–10% of all lymphomas [1]. Moreover, the incidence of MCL has been increasing over the last decade, especially among elderly patients [2]. While extensive research has been exploring new and better ways to treat MCL, the histological diagnosis is invariably difficult and normally requires immunophenotyping; this is required even though MCL has been established as a new disease entity characterized by the t(11;14)(q13;q32) [3]. In particular, MCL is considered a heterogeneous disease on the basis of its development, growth, and prognosis [4]. The effect of chemotherapy also seems to vary depending on the tumor biology [5]. Clinically, the majority of patients present in an advanced stage, and up to 80% include the involvement of extranodal sites [6, 7]. These factors eventually lead to an aggressive clinical course, associated with rapid progression and a high recurrence rate. In Korea, MCL accounts for 2% of B-cell lymphomas, and it is typically characterized by an aggressive clinical course [8]. However, little is known about the clinical features and treatment outcomes in MCL patients in Korea.

Determining the optimal prognostic model for MCL is quite difficult owing to its rarity and diverse clinical course. Several studies have demonstrated that various prognostic factors are associated with survival in patients with MCL. For example, older age, elevated lactate dehydrogenase (LDH), advanced stage, presence of B symptoms, poor performance status, and high mitotic index (Ki-67) are often associated with poor prognosis [9, 10]. Recently, a simplified MCL Prognostic Index (MIPI) scoring system incorporating age, performance status, LDH level, and WBC count, has been established as a new prognostic model to predict the survival outcome for patients with MCL [11]. However, this index still requires validation when taking tumor and racial differences into consideration.

Although various chemotherapeutic regimens show significant activity in patients with MCL, no regimen has been found to be superior, and no standard treatment has been identified. Rituximab is a chimeric monoclonal antibody against the protein CD20, which is primarily found on the surface of malignant B-cells. The addition of rituximab to cyclophosphamide, doxorubicin, vincristine, and prednisolone (R-CHOP) has led to an impressive improvement in response rates and survival outcomes for patients with diffuse large B-cell lymphoma [12]. Several recent studies have also demonstrated that including rituximab in combination chemotherapy produces a significantly improved therapeutic effect for MCL [9, 13]. Other studies have also shown that rituximab can alleviate the negative impact of extranodal involvement [14]. Nevertheless, it is uncertain whether rituximab-based chemotherapy alters the clinical outcomes of patients with MCL.

As there is a lack of available data in this area, this study sought to provide basic clinical data for prospective clinical trials by evaluating the clinical features and treatment outcomes for patients with MCL in Korea.

MATERIALS AND METHODS

Patients and treatment

A retrospective review of the medical records of 131 patients who were newly diagnosed with MCL between January 2004 and December 2009 at 15 medical centers in Korea was conducted. Each medical center received unified case report forms. The collected data included the age, gender, performance status, presence of B symptoms (fever, night sweats, and weight loss), presence of extranodal disease, International Prognostic Index (IPI) score [15], simplified MIPI score [11], serum LDH, hemoglobin (Hb), WBC, platelets (Plt), initial date of diagnosis, and treatment modality utilized. All patients were evaluated by using standard laboratory tests, computed tomography (CT), bone marrow (BM) aspirate and biopsy, and endoscopy at diagnosis. Standard institutional protocols were used for central nervous system (CNS) prophylaxis. All patients were staged according to the Ann Arbor Staging classification by using CT scans [16]. Strict histologic and recently updated criteria were applied, and only patients with a confirmed MCL diagnosis were included in the study [17]. Cyclin D1 overexpression was present in 99/101 cases (98.0%), and CD5 overexpression was present in 68/86 cases (79.1%). The Ki-67 index was assessed in 57 cases (43.5%). Additional data obtained included the time to relapse, salvage treatment modality, and survival rates with salvage treatment. This study was approved by the institutional review board of each center.

Statistical analysis

The descriptive statistics are reported as the proportion and median. The response was evaluated by using revised response criteria for malignant lymphomas [18]. Overall survival (OS) was defined as death from any cause from the time of diagnosis. Event-free survival (EFS) was defined as the time from diagnosis to failure or death from any cause. The OS and EFS were analyzed by using the Kaplan-Meier test, and each group was compared by using a log-rank test. The Cox regression model was used to determine the clinical predictors for EFS and OS. An effect was considered statistically significant when $P<0.05$. All analyses were performed by using the Statistical Package for the Social Sciences (SPSS) software version 14 (SPSS Inc., Chicago, IL, USA).

RESULTS

Clinical features and characteristics

The total cohort included 131 patients (Table 1). The median age was 63 years (range, 26–78 years), and 77.9% were men. A total of 105 patients (80.1%) had stage III or IV MCL at diagnosis. On the basis of the IPI, 52 patients (39.7%) were categorized with high- or high-intermediate risk MCL.

Table 1. Baseline characteristics of patients.

	Total patients (N=131)
Age (yr)	63 (26–78)
Gender	
Men	102 (77.9)
Women	29 (22.1)
ECOG score	
0	34 (26.0)
1	86 (65.6)
2–4	11 (8.4)
Stage	
I	9 (6.9)
II	17 (13.0)
III	35 (26.7)
IV	70 (53.4)
IPI	
Low	30 (22.9)
Low-intermediate	49 (37.4)
High-intermediate	35 (26.7)
High	17 (13.0)
Simplified MIPI	
Low	51 (38.9)
Intermediate	41 (31.3)
High	18 (13.7)
Unknown	21 (16.0)
B symptom	34 (26.0)
Extranodal involvement	91 (69.5)
BM involvement	54 (41.2)
GI involvement	46 (35.1)
CNS involvement	11 (8.4)
Lung involvement	8 (6.1)
Liver involvement	5 (3.8)

Values are presented as numbers (%).
Abbreviations: ECOG, Eastern Cooperation Oncology Group; IPI, International Prognostic Index; MIPI, MCL International Prognostic Index; BM, bone marrow; CNS, central nervous system; GI, gastrointestinal tract.

Table 2. Types of first-line treatment.

	Total patients (N=131)
Rituximab-containing regimen	71 (54.2)
R-CHOP	54 (41.2)
R-CHOP-like regimen	2 (1.5)
RHyperCVAD/RMTX-Ara-C	10 (7.6)
RCVP	2 (1.5)
RICE	1 (0.8)
RESHAP	2 (1.5)
Non-rituximab-containing regimen	60 (45.8)
CHOP	23 (17.6)
CHOP-like regimen	2 (1.5)
HyperCVAD/MTX-Ara-C	18 (13.8)
CVP	6 (4.5)
ESHAP	5 (3.8)
ESHAP-like regimen	1 (0.8)
Fludarabine-based regimen	4 (3.1)
GIDOX	1 (0.8)

Values are presented as numbers (%).
Abbreviations: R-CHOP, rituximab, cyclophosphamide, doxorubicin, and prednisone; RHyperCVAD/RMTX-Ara-C, rituximab, doxorubicin, vincristine, dexamethasone, methotrexate, and cytarabine; RCVP, rituximab, cyclophosphamide, vincristine, and prednisone; RICE, rituximab, ifosfamide, carboplatin, and etoposide; RESHAP, rituximab, etoposide, methylprednisone, cytarabine, and cisplatin; CHOP, cyclophosphamide, doxorubicin, and prednisone; HyperCVAD/MTX-Ara-C, doxorubicin, vincristine, dexamethasone, methotrexate, and cytarabine; CVP, cyclophosphamide, vincristine, and prednisone; ICE, ifosfamide, carboplatin, and etoposide; ESHAP, etoposide, methylprednisone, cytarabine, and cisplatin; GIDOX, gemcitabine, ifosfamide, dexamethasone, and oxaliplatin.

According to the simplified IPI, 18 patients (13.7%) were at high risk. B symptoms were noted in 34 patients (26.0%). The overall incidence of extranodal involvement was 69.5%. The most common extranodal sites were the BM (52.8%) and the gastrointestinal (GI) tract (34.7%); other extranodal sites included the CNS (8.4%), lungs (6.1%), liver (3.8%), and spleen (3.8%).

First-line treatments and outcomes

No patients were pretreated. As expected, the treatments were heterogeneous (Table 2). R-CHOP was frequently used as the first-line treatment (41.2%). Ten patients (7.6%) received rituximab plus hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone alternating with methotrexate-cytarabine (RHyperCVAD/RMTX-Ara-C). Seventy-one patients (54.2%) were treated with a rituximab-containing regimen, while 60 patients (45.8%) received a non-rituximab-containing regimen.

The treatment outcomes are shown in Table 3. A total of 121 patients were evaluated. The complete response (CR) and partial response (PR) rates were 45.0% and 27.5%, respectively. Overall, 73 patients experienced relapse, and

Table 3. Treatment outcomes of patients.

	Total patients (N=131)
Response to first-line treatment	
CR	59 (45.0)
PR	36 (27.5)
SD	2 (1.5)
PD	14 (10.7)
Unknown	20 (15.3)
Survival status	
Relapse	73 (55.7)
Salvage treatment	66 (50.4)
Fludarabine-based chemotherapy	17 (13.0)
Cytarabine-containing chemotherapy	30 (22.9)
CHOP/CHOP-like chemotherapy	5 (3.8)
CVP	3 (2.3)
ICE	3 (2.3)
Other chemotherapy	8 (6.1)
Death	65 (49.6)
Alive	55 (42.0)
Unknown	11 (8.4)

Values are presented as numbers (%).
Abbreviations: CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; CHOP, cyclophosphamide, doxorubicin, and prednisone; CVP, cyclophosphamide, vincristine, and prednisone; ICE, ifosfamide, carboplatin, and etoposide.

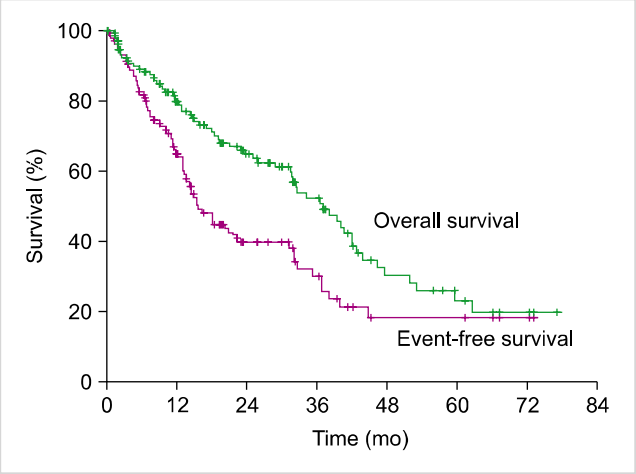

Fig. 1. Kaplan-Meier analysis of overall survival and event-free survival.

65 patients died. Among the relapsed patients, 66 received salvage treatment. The salvage regimens were heterogeneous, with 17 patients receiving fludarabine-based chemotherapy and 30 patients receiving cytarabine-containing chemotherapy.

Survival

With a median follow-up duration of 20.0 months (range, 0.2–77.0 months), the OS at 2 years was 64.7%, while the EFS was 39.7% (Fig. 1). As seen in Figs. 2 and 3, the IPI and MIPI had a statistically significant effect on OS (P=0.045 and $P<0.001$, respectively). Achieving CR was significantly associated with the OS ($P<0.001$). Among 57 patients, the Ki-67 index was significantly associated with the EFS (P=0.016). In the univariate and multivariate analyses for EFS and OS, the simplified MIPI was significantly associated with OS (Table 4). Simplified MIPI had a statistically meaningful impact on OS in patients who did not receive ritux-

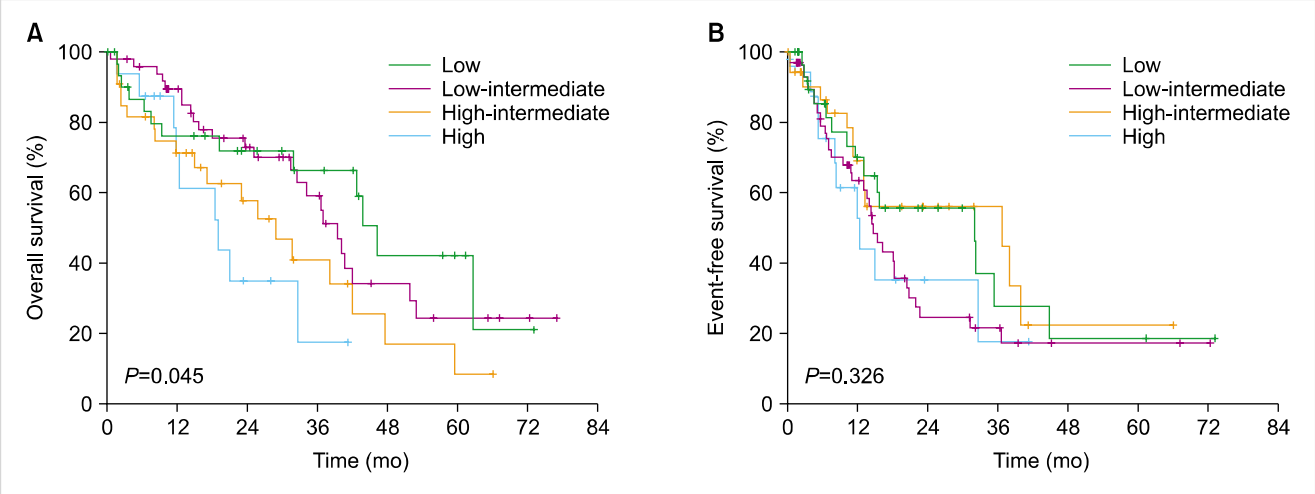

Fig. 2. Kaplan-Meier analysis of **(A)** overall survival and **(B)** event-free survival based on the International Prognostic Index.

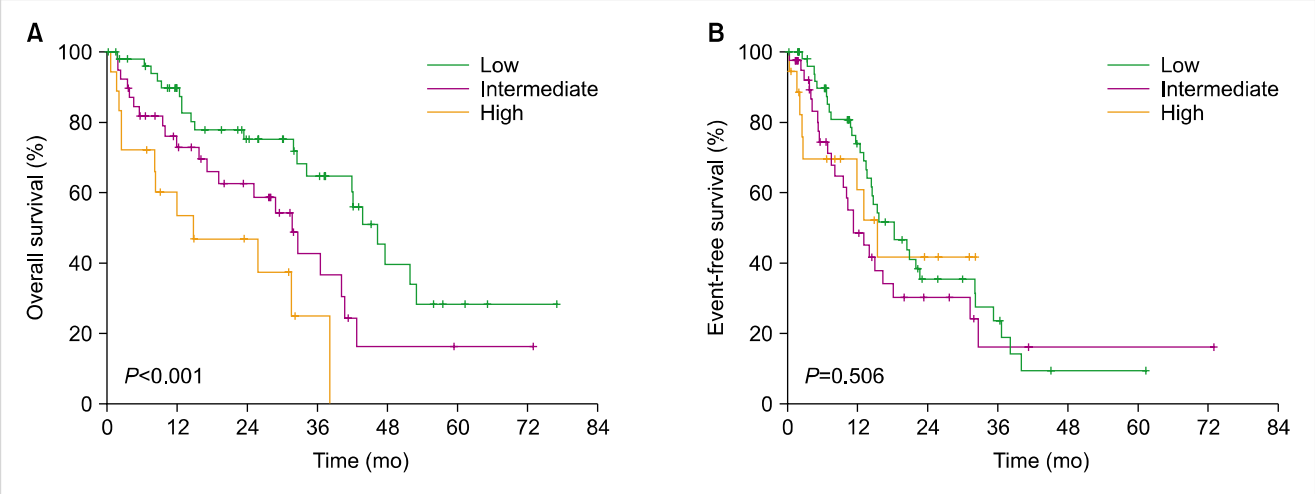

Fig. 3. Kaplan-Meier analysis of **(A)** overall survival and **(B)** event-free survival based on the Mantle Cell Lymphoma International Prognostic Index.

Table 4. Univariate and multivariate analyses for factors affecting EFS and OS.

Factor	$P^{a)}$	EFS			$P^{a)}$	OS		
		HR	95% CI	*P*		HR	95% CI	*P*
Gender (men)	0.443	0.749	0.403–1.392	0.360	0.345	1.533	0.807–2.913	0.192
Stage III/IV	0.114	2.295	1.144–4.606	0.019	0.117	2.102	0.981–4.507	0.056
B symptoms (+)	0.664	1.339	0.350–1.034	0.066	0.691	1.811	0.958–3.422	0.067
Extranodal involvement (+)	0.245	0.601	0.350–1.034	0.338	0.812	0.952	0.516–1.759	0.876
Use of rituximab-containing regimen	0.293	1.595	0.926–2.749	0.093	0.577	0.891	0.514–1.542	0.679
Simplified MIPI (intermediate/high)	0.506	1.344	0.814–2.220	0.248	<0.001	2.393	1.327–4.316	0.004

[a)]Log-rank test for univariate analysis.
Abbreviations: HR, hazard ratio; MIPI, MCL International Prognostic Index; EFS, event-free survival; OS, overall survival; CI, confidence interval.

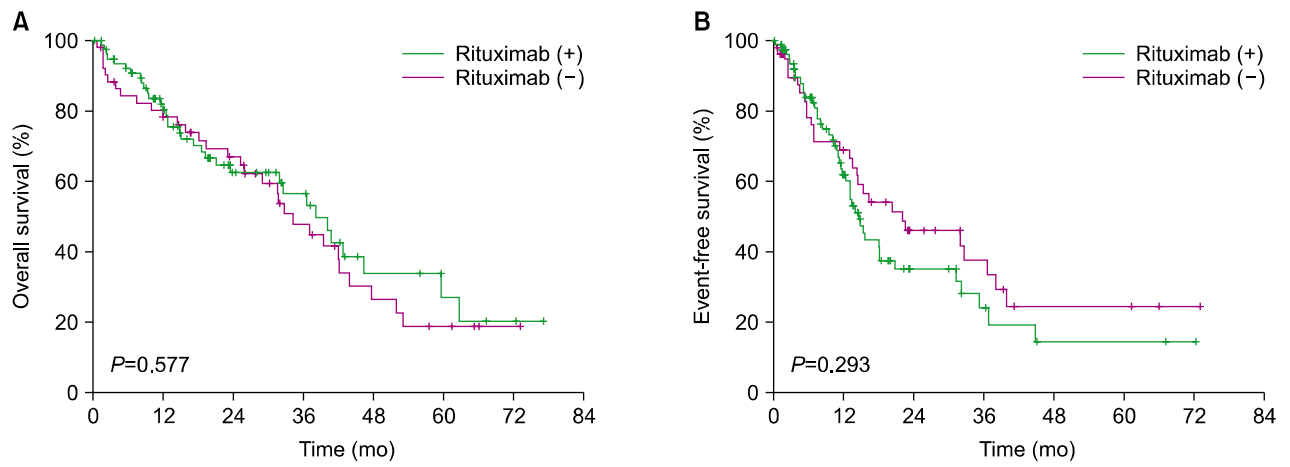

Fig. 4. Kaplan-Meier analysis of **(A)** overall survival and **(B)** event-free survival based on rituximab-containing therapy as the first-line treatment.

imab-containing treatments ($P<0.001$) and showed a better OS in patients who received rituximab-containing treatments ($P=0.083$). However, the use of rituximab-containing treatments was not associated with OS and EFS (Fig. 4).

DISCUSSION

MCL is characterized by an aggressive clinical course, and there is a pattern of frequent relapse after conventional chemotherapy. However, recent novel treatment options, such as rituximab and transplantation, have improved the response and survival outcomes [9]. As a result, the prognosis and survival of patients with MCL have considerably improved recently [5]. In addition, the significant improvement in treatment outcomes observed with the introduction of rituximab has altered the risk assessment for MCL. Therefore, an in-depth analysis of patients with MCL is important to help identify more adequate initial treatment modalities.

The present study found similar clinical characteristics to those reported previously. The patients in the current study had a median age of approximately 63 years and were predominantly men with mostly advanced stage MCL and frequent extranodal involvement, including the BM in the majority of cases [4, 7, 19-22]. GI involvement was observed in 35.1% of the patients, which is similar to the rate described in other studies [19, 23]. In addition, several studies have demonstrated that consideration of MCL with GI involvement is important in the treatment planning, response assessment, and surveillance of patients with lymphoma [24, 25]. However, in contrast to other studies, the incidence of CNS involvement in the current study was relatively low. This discrepancy may be due to a lack of actual CNS examinations and a possible underestimation of CNS involvement. Indeed, the use of routine CNS examinations and prophylaxes remains controversial [16]. Similar to previous studies, other extranodal sites included the lungs, liver, and spleen, although these locations are considered rare [14, 26].

While a median survival of approximately 3 years has been common in previous reports, this has recently increased to 5 years [3]. Herrmann *et al.* [5] suggested that such superior outcomes may be a result of different patient selection, improved diagnosis, and improved treatment. In the current study, the 5-year OS rate was 23.1%, with a continuous decline of the survival curve. Although the addition of rituximab has improved the response rate and time-to-failure

in the first-line setting, this has not translated into significant improvement in the OS. The results of the present study indicate that patients with MCL have a poor prognosis, even after rituximab-based chemotherapy [27]. Most patients in the current study also had poor clinical factors, such as advanced age, poor performance status, multiple extranodal involvements, and B symptoms at diagnosis. In addition, 45.8% of patients did not receive rituximab-based chemotherapy as a first-line treatment. The CR rate was 45.0%, which is similar to the results from other studies, where CR rate ranged from 30% to 80% [28]. The current study also showed that achieving CR prolonged OS. After relapse, the median life expectancy for a patient with MCL drops to 1–2 years [9]. Once relapse occurs, patients are offered aggressive chemotherapy; however, standard salvage chemotherapy has not yet been defined.

This study sought to provide an in-depth report on MCL subgroups with significantly worse clinical outcomes. Several previous studies have identified prognostic factors for MCL. While the IPI is a powerful tool for predicting clinical outcomes in patients with aggressive non-Hodgkin lymphoma [15], only a few studies have used IPI for predicting and examining MCL prognosis. However, a specific MCL prognostic score was recently proposed, and this score identifies 4 independent prognostic factors [11]. In terms of prognostic factors, the MIPI was found to correlate with OS in the current study including Korean patients. Older age and poor performance status are commonly mentioned as negative predictive factors for survival in cases of MCL [6, 11, 21]. Interestingly, patients with MCL and B symptoms displayed a worse survival trend. This agrees with previous reports showing that B symptoms have a negative impact on survival [29].

In conclusion, the present data reveal the clinical features and treatment outcomes for patients with MCL in Korea who received at least 1 chemotherapeutic regimen. Similar to the results from Western countries, patients with MCL in Korea were characterized by the aggressive clinical features and particularly poor clinical outcomes. The simplified MIPI was an important prognostic factor in patients with MCL in Korea. Although MIPI was a prognostic factor in the current study, an analysis of prognostic subgroups should be evaluated and validated for patients with MCL. In addition, rituximab did not significantly improve the therapeutic effect in patients with MCL in Korea; therefore, a more suitable treatment needs to be identified for patients with MCL in Korea.

ACKNOWLEDGMENTS

All authors collaborated in the collection and interpretation of the data and contributed to the manuscript.

Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

REFERENCES

1. Zhou Y, Wang H, Fang W, et al. Incidence trends of mantle cell lymphoma in the United States between 1992 and 2004. Cancer 2008;113:791-8.
2. Aschebrook-Kilfoy B, Caces DB, Ollberding NJ, Smith SM, Chiu BC. An upward trend in the age-specific incidence patterns for mantle cell lymphoma in the USA. Leuk Lymphoma 2013;54:1677-83.
3. Ghielmini M, Zucca E. How I treat mantle cell lymphoma. Blood 2009;114:1469-76.
4. Chim CS, Chan AC, Choo CK, Kwong YL, Lie AK, Liang R. Mantle cell lymphoma in the Chinese: clinicopathological features and treatment outcome. Am J Hematol 1998;59:295-301.
5. Herrmann A, Hoster E, Zwingers T, et al. Improvement of overall survival in advanced stage mantle cell lymphoma. J Clin Oncol 2009;27:511-8.
6. Leitch HA, Gascoyne RD, Chhanabhai M, Voss NJ, Klasa R, Connors JM. Limited-stage mantle-cell lymphoma. Ann Oncol 2003;14:1555-61.
7. Oinonen R, Franssila K, Teerenhovi L, Lappalainen K, Elonen E. Mantle cell lymphoma: clinical features, treatment and prognosis of 94 patients. Eur J Cancer 1998;34:329-36.
8. Ko YH, Kim CW, Park CS, et al. REAL classification of malignant lymphomas in the Republic of Korea: incidence of recently recognized entities and changes in clinicopathologic features. Hematolymphoreticular Study Group of the Korean Society of Pathologists. Revised European-American lymphoma. Cancer 1998;83:806-12.
9. Goy A, Kahl B. Mantle cell lymphoma: the promise of new treatment options. Crit Rev Oncol Hematol 2011;80:69-86.
10. Tiemann M, Schrader C, Klapper W, et al. Histopathology, cell proliferation indices and clinical outcome in 304 patients with mantle cell lymphoma (MCL): a clinicopathological study from the European MCL Network. Br J Haematol 2005;131:29-38.
11. Hoster E, Dreyling M, Klapper W, et al. A new prognostic index (MIPI) for patients with advanced-stage mantle cell lymphoma. Blood 2008;111:558-65.
12. Coiffier B. Rituximab in diffuse large B-cell lymphoma. Clin Adv Hematol Oncol 2004;2:156-7.
13. Williams ME, Connors JM, Dreyling MH, et al. Mantle cell lymphoma: report of the 2010 Mantle Cell Lymphoma Consortium Workshop. Leuk Lymphoma 2011;52:24-33.
14. Ferry JA. Extranodal lymphoma. Arch Pathol Lab Med 2008;132:565-78.
15. A predictive model for aggressive non-Hodgkin's lymphoma. The International Non-Hodgkin's Lymphoma Prognostic Factors Project. N Engl J Med 1993;329:987-94.
16. Armitage JO. Staging non-Hodgkin lymphoma. CA Cancer J Clin 2005;55:368-76.
17. Sabattini E, Bacci F, Sagramoso C, Pileri SA. WHO classification of tumours of haematopoietic and lymphoid tissues in 2008: an overview. Pathologica 2010;102:83-7.
18. Cheson BD, Pfistner B, Juweid ME, et al. Revised response criteria

for malignant lymphoma. J Clin Oncol 2007;25:579-86.
19. Bertini M, Rus C, Freilone R, et al. Mantle cell lymphoma: a retrospective study on 27 patients. Clinical features and natural history. Haematologica 1998;83:312-6.
20. Bosch F, Lopez-Guillermo A, Campo E, et al. Mantle cell lymphoma: presenting features, response to therapy, and prognostic factors. Cancer 1998;82:567-75.
21. Kauh J, Baidas SM, Ozdemirli M, Cheson BD. Mantle cell lymphoma: clinicopathologic features and treatments. Oncology (Williston Park) 2003;17:879-91, 896.
22. Weisenburger DD, Vose JM, Greiner TC, et al. Mantle cell lymphoma. A clinicopathologic study of 68 cases from the Nebraska Lymphoma Study Group. Am J Hematol 2000;64:190-6.
23. Romaguera JE, Medeiros LJ, Hagemeister FB, et al. Frequency of gastrointestinal involvement and its clinical significance in mantle cell lymphoma. Cancer 2003;97:586-91.
24. Chung Kim Yuen C, Tomowiak C, Yacoub M, Barrioz T, Barrioz C, Tougeron D. A rare case of mantle cell lymphoma as lymphomatous polyposis with widespreadinvolvement of the digestive tract. Clin Res Hepatol Gastroenterol 2011;35:74-8.
25. Sikalias N, Alexiou K, Demonakou M, Mylona SC, Papadaki T, Ekonomou N. Non-polypoidal, synchronous mantle-cell lymphoma of small intestine: a rare case. World J Surg Oncol 2010;8:69.
26. Molina TJ, Delmer A, Cymbalista F, et al. Mantle cell lymphoma, in leukaemic phase with prominent splenomegaly. A report of eight cases with similar clinical presentation and aggressive outcome. Virchows Arch 2000;437:591-8.
27. Lenz G, Dreyling M, Hoster E, et al. Immunochemotherapy with rituximab and cyclophosphamide, doxorubicin, vincristine, and prednisone significantly improves response and time to treatment failure, but not long-term outcome in patients with previously untreated mantle cell lymphoma: results of a prospective randomized trial of the German Low Grade Lymphoma Study Group (GLSG). J Clin Oncol 2005;23:1984-92.
28. Hess G. New combinations for mantle cell lymphoma: concerted action needed. Lancet Oncol 2011;12:315-6.
29. Vose JM. Mantle cell lymphoma: 2012 update on diagnosis, risk-stratification, and clinical management. Am J Hematol 2012;87:604-9.